

R E M A R K S

The Applicants acknowledge the Office Action, a FINAL REJECTION, with appreciation. Claims 25, 27, 28, 30, 31 and 35-48 are pending in the application. Claims 40-48 are withdrawn from consideration. The Applicants request rejoinder of the withdrawn subject matter upon the Office determination of allowable subject matter in the elected invention. Claims 25, 27, 28, 30, 31 and 35-39 remain under consideration.

To begin, the Office maintains the objection to the Specification made in paragraph 8 of the Office Action of August 29, 2003. The Applicants acknowledge the Office objection as to the Specification format and comment that we will, in the future, strive to conform to this non-mandatory requirement. Moreover, the Applicants acknowledge the Office notation that the Specification makes reference to substances which are identified by their registered trademarks. The Applicants will, in the future, strive to conform to this non-mandatory requirement.

The Office acknowledges our Response and Amendment of December 1, 2003, as well as our Response to the Office Communication of March 10, 2004. With the instant Office Action, the elected claims 25, 27, 28, 30, 31 and 35-39 are properly examined based on the amendments made in the Response and Amendment of December 1, 2003 and the Supplemental Response and Amendment of June 28, 2004.

Rejections under 35 U.S.C. § 112, first and second paragraphs, have been rendered moot or have been withdrawn in light of the amendments made with the Response and Amendment of December 1, 2003. The Office formulates new rejections under 35 U.S.C. § 112. The prior art rejections under 35 U.S.C. § 102 have been withdrawn; however, the Office articulates modified rejections with the instant Office Action.

The Office rejects Claims 25, 27, 28, 31 and 35-39 under 35 U.S.C. § 112, second paragraph, for failing to claim with particularity. The Office opines that Claim 25 is confusing and/or lacks proper antecedence. With the Response After Final, the

Applicants amend Claims 25, 38 and 39 to include the language which refers to a "biologically active substance", as kindly suggested by the Office.

With the Response After Final, the Applicants amend base Claim 25 to clearly set forth that the coupled biologically active substance is internalized into the antigen-presenting cells. There exists Specification support for the clarifying language regarding the internalization of the coupled biologically active substance.

Consequently, this language may not be considered to be new matter. In the Office Action of August 29, 2003 (page 7, paragraph 10), the Office concludes that the Specification is enabled for a process of using the OmpA protein having the amino acid sequence of SEQ ID NO:2 in the preparation of a composition wherein the OmpA has the ability internalize into dendritic cells or bind specifically to dendritic cells, monocytes, or B lymphocytes. Thus, the instant amendment including the language directed to the internalization of the coupled biologically active substance is enabled by the Specification disclosure as articulated by the instant Examiner.

With the Response and Amendment of December 1, 2003 (pages 5-6), the Applicants distinguish the instant method of delivering a biologically active substance to antigen-presenting cells, in part, by the internalization of the coupled biologically active substance. As noted by the instant Examiner, the claimed method does not include language directed to the step of 'internalization into the APC'. The Applicants submit that the instant amendment provides a claimed distinction over the cited prior art and obviates the rejections under 35 U.S.C. §§ 102(a) and 102(b).

The Applicants submit that the instant amendment to Claim 25, including the language directed to the coupled biologically active substance being internalized into the antigen-presenting cells, distinguishes over the cited prior art which do not literally disclose binding and internalization of rP40 complexes. Although not literally disclosed, the Office may not conclude that contacting of the biologically active complex to antigen-presenting cells and subsequent internalization of the complex is inherent to the immune mechanism of rP40 complexes. Internalization of the active complex by antigen-presenting cells is not an inherent characteristic of

rP40. In other words, simply contacting the cell with the biologically active complex does not necessarily lead to internalization of the complex. In support this concept, the Applicants demonstrate internalization of the rP40 in Example 7, page 20, of the instant Specification. The Applicants also demonstrate that under different conditions, the protein is not internalized by the cells, but instead is bound to the cell surface. Therefore, cellular internalization is not an intrinsic consequence or an inherent characteristic of the rP40 following contact with antigen-presenting cells and is therefore, not anticipated by the prior art of record.

For response to the Final Rejection, the Applicants provide the following arguments rebutting the individual modified rejections and, in view of the instant amendment, drawn to the coupled biologically active substance being internalized into the antigen-presenting cells.

The Office rejects Claims 25, 27, 28, 31 and 35-39 under 35 U.S.C. § 102(a) as being anticipated by Andreoni, et al., (WO 99/49892A2). The Office concludes that contacting the coupled biologically active substance with the antigen-presenting cells is an inherent property of the rP40 disclosed in Andreoni, et al. given that the rP40 comes in contact with antigen-presenting cells *in vivo* in the mammal to generate immunity.

To further distinguish the instant invention from Andreoni, et al., the Applicants amend Claim 25 to include claim language explaining that the coupled biologically active substance is internalized into the antigen-presenting cells upon contacting the cells. The disclosure of Andreoni, et al. does not anticipate that rP40 complexes may be internalized by antigen-presenting cells. As discussed previously, internalization of the coupled biologically active substance is not an inherent characteristic of OmpA following contacting with antigen-presenting cells, and, consequently, not part of such disclosure. Reconsideration and withdrawal of the prior art rejection is respectfully solicited.

The Office rejects Claims 25, 27, 28, 31 and 35-39 under 35 U.S.C. § 102(b) as being anticipated by Binz, et al., (WO 97/41888-A1). The Office considers Binz, et al. to teach a method of delivering a *Klebsiella pneumnoniae* membrane protein (rP40), with a biologically active substance associated with it, to popliteal lymph nodes of rabbits. The Office concludes that by injecting the coupled substance into the popliteal lymph node, the complex inherently contacts the antigen-presenting cells and delivers the biologically active substance to the antigen-presenting cells, and thereby, anticipates all the elements of the claims.

The instant amendment of Claim 25 to include claim language explaining that the coupled biologically active substance is internalized into the antigen-presenting cells also distinguishes the instant method over the cited Binz, et al. disclosure. Binz, et al. does not disclose, literally or inherently, that rP40 complexes may be internalized by antigen-presenting cells, see previous notes. Reconsideration and withdrawal of the rejection for anticipation is respectfully requested.


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Accordingly, entry of the present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,
THE FIRM OF HUESCHEN AND SAGE

By: 
G. PATRICK SAGE, #37,710

Dated: January 7, 2005
Customer No.: 25,666
500 Columbia Plaza
350 East Michigan Ave.
Kalamazoo, MI 49007-3856
(269) 382-0030

Enclosure: Listing of Claims, Extension Fee (one month) \$120.00 and Postal Card
Receipt.

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**THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER
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